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Predicting COVID-19 outcomes from clinical and laboratory parameters in an intensive care facility during the second wave of the pandemic in South Africa

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Highlights

- Data from Africa on COVID-19 second wave are scarce
- Clinical presentations of COVID-19 severity in the ICU during the second wave
- Predicting COVID-19 progression outcomes based on clinical and laboratory data
- D-dimer, TropT, NTProbBNP and CRP and HCO3std as COVID-19 mortality risk factors

Title: Predicting COVID-19 outcomes from clinical and laboratory parameters in an intensive care facility during the second wave of the pandemic in South Africa

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Abstract

Abstract

Background: The second wave of COVID-19 in South Africa was caused by the Beta variant of SARS-CoV-2. This study aimed to explore clinical and biochemical parameters that could predict COVID-19 patients' outcome.

Methods: We conducted a prospective study between 05 November 2020 and 30 April 2021 among confirmed COVID-19 patients admitted to the intensive care unit (ICU) of a tertiary hospital. We used cox proportional hazards model in Stata 16 to assess the risk factors associated with discharge or death. Those factors with $p< 0.05$ were considered statistically significant.

Results: We found a significantly 'low median pH ($p<0.001$)', 'increased median arterial partial pressure of carbon dioxide ($p<0.001$)', 'elevated "D-dimer ($p=0.003$)', ''elevated 'Troponin T ($p=0.003$)', 'N-terminal (NT)-prohormone BNP ($p=0.010$)', and 'C-reactive protein ($p = 0.013$)'" among COVID-19 patients who died as opposed to those who were discharged. An increased HCO3std was associated with a lower risk of death (HR 0.96, 95%CI: 0.93-0.99).

Conclusions: The mortality of COVID-19 patients admitted to ICU was associated with elevated D-dimer and TropT, low HCO3std. In addition, patients who died had a shorter duration of ICU stay. Large studies are warranted to increase identification of patient at risk of poor prognosis and improve clinical approach.

Keywords: COVID-19, SARS-CoV-2, mortality, ICU, second wave, Biomarkers,

1. Introduction

The novel coronavirus disease 2019 (COVID-19) pandemic has caused over 472 million cases with 6,09 million deaths worldwide as of March 24th, 2022 (WHO, 2022). Due to the continuous transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) around the world, mutations of the virus led to a wave of COVID-19 (Fontanet et al., 2021; Mascola et al., 2021; Zhang et al., 2021). One of these mutations was designated as the Beta variant. It was reported to be more transmissible with concerns that this strain would be resistant to the vaccine which was developed based on the original SARS-CoV-2 strain (Mascola et al., 2021; Tegally et al., 2021). The Beta variant was first reported in the Eastern Cape province of South Africa in October 2020 (Tegally et al., 2021) and spread to neighbouring countries like Botswana, as well as globally (Tang et al., 2021; Tang et al., 2021a).

A study of the second wave in Vietnam reported that fewer older people with a mean age of 46 years and that more females were infected (Nong et al., 2021). Comparative studies of the first and second waves found a variation in the difference in mortality between the first two waves. While some studies show that the second wave had more incident cases than the first wave, including static numbers of intensive care unit (ICU) admission and deaths (Coccia, 2021; Salyer et al., 2021), other studies show a reduction in mortality during the second wave (Nong et al., 2021; James et al., 2021; Fan et al., 2021).

In Africa, as of the 31st of December 2020, 40 countries were already experiencing their second wave with the continent reporting a mean of 23790 daily new cases for epidemiological week 53 (Salyer et al., 2021). South Africa was the most severely

affected African country with over 80000 deaths by the end of December 2020, experiencing the start of the second wave in October 2020 (Frean, 2021). The Western Cape, Eastern Cape, and KwaZulu–Natal provinces were most affected by the second wave, with the Western Cape Province reaching peak infection levels higher than that of the first wave (Tegally et al., 2021; Frean, 2021). A national analysis of data from the daily hospital surveillance (DATCOV) national active surveillance system for COVID-19 hospitalisations concurred, as it showed that individuals hospitalised in the second wave were more likely to be older; more than 40 years, and less likely to have comorbidities (Jassat et al., 2021). It concluded that there was a higher incidence of positive cases, an increase in hospitalization, and increased in-hospital mortality in the second wave, compared to the first wave (Jassat et al., 2021). Identification of specific clinical and laboratory biomarkers of high mortality risk may improve decision-making for COVID-19 management in clinical practice. We conducted a prospective study between 05 November 2020 and 30 April 2021, of patients with COVID-19 admitted to the ICU to define clinical features and laboratory biomarkers associated with an increased risk of mortality in COVID-19 patients admitted in the ICU at a tertiary hospital in the Western Cape Province during the second wave in South Africa.

2. Methods

2.1. Study population

The study was conducted at Tygerberg Hospital, a 1380-bed tertiary hospital in Cape Town. The hospital provides tertiary services to approximately 3.5 million people from the Western Cape Province. Much of the population serviced by the hospital are from low-

income areas, with a significant proportion living in low-cost and informal settlements where overcrowding, shared ablution and water facilities make social distancing and the advocated hygiene methods difficult. The study population comprised all consecutive patients admitted to the adult ICU between 05 November 2020 to 30 April 2021, when the database was censored. Over the course of the pandemic, the ICU's capacity fluctuated. According to provincial guidelines, patients referred to the ICU were triaged by the consultants on duty based on disease severity and likely prognosis, and admissions were contingent on bed availability (CCSSA, 2021).

2.2. Data collection

Data were captured prospectively each day using photographs of bedside clinical notes, which were securely stored electronically. Clinical data were remotely entered by a data-capturer into the Redcap® database, while laboratory results were also imported from the National Health Laboratory Services (NHLS) into the database. The data was quality checked by the 'data entry supervisor' to ensure that the information entered was of high quality and reliable.

2.3. Outcomes and predictors variables

Data collected included sociodemographic (age, sex, socio-economic status); clinical disease characteristics, pre-existing comorbidities (hypertension, diabetes, cardiovascular disease (CVD), chronic lung disease, obesity, and Human Immunodeficiency Virus (HIV)); routinely collected laboratory data; mode of respiratory support and management strategy. The primary outcome of interest was the proportion

of patients who died after admission in the ICU, including those who were discharged from ICU and those who died in hospital. Time to death or censored (alive at discharge) was also assessed.

2.4. Statistical analysis

Continuous variables were expressed as median with inter-quartile range for skewed data. Categorical variables were expressed using frequencies and percentages. A multivariable model was developed for demographics, comorbidities, drugs, clinical symptoms, and bio-chemical parameters using variables strongly associated with mortality or survival outcomes at univariable analysis. The comparison between mortality and survival used the Pearson $\chi 2$ test or Fisher exact test where appropriate for categorical variables, and the Wilcoxon's rank-sum test for continuous variables. Factors associated with death or survival at p-value < 0.05 in unadjusted univariable were considered as statistically significant. To compare the survival functions for each socio-demographic, clinical, and biochemical covariate, the log-rank test, and the Wilcoxon test were used. Hazard ratios (HRs) were calculated using Cox's proportional hazards model to assess the risk factors associated with discharge and death. All statistical analyses were performed using Stata (V.16, Stata Corp, College Station, Texas, USA) statistical software.

3. Results

In this cohort, 82 patients were admitted to the ICU from 5 November to April 2021. Among them, 27 (33%) were males. Table 1 compared patient characteristics among

those who died or survived while admitted to ICU. The median age (IQR) of those who were discharged was not significantly different from those who died: 50.4 (39.9-60.5) vs 55.2 (47.2-58.1), (p = 0.497). Underlying comorbidities were hypertension (48%), diabetes mellitus (41%), HIV (11%), hyperlipidemia (6%), and asthma (2%) (Table 1). The median duration of stay in ICU was 12 days (IQR: 8-17) days. The most common clinical features at presentation included fever (30%) and myalgia (29%) (Table 1).

The median pH was 0.07 lower among those who died than discharged patients ($p<0.001$), whereas the median $PaCO_2$ was 0.95 kPa higher among those who died ($p<0.001$) (Table 1). Comparing the D-dimer between patients who died and those who survived, the median (IQR) of D-dimer was 1.51 (0.65-4.86) versus 0.41 (0.24-0.95), $p<0.001$ respectively (Table 1). Lastly, baseline biochemical parameters namely median Troponin T (TropT), N-terminal pro B-type natriuretic peptide (NT-proBNP) and C-reactive protein (CRP) were significantly higher among patients who died (18 versus 6, p = 0.001), (254.50 versus 110, p = 0.007) and (167.50 versus 106.00, p = 0.010), respectively (Table 1).

The multivariate Cox proportional hazard model was performed to assess the relationship between various covariates and patients' survival or the risk of death. Data shows that elevated D-dimer levels were associated with increased risk of mortality in ICU (HR 1.05, 95%CI 1.00. -1.11); and elevated HCO3std level were associated with lower risk of mortality (HR 0.96, 95% CI 0.93-0.99). Furthermore, an increased lymphocyte count was associated with an increased in probability of being discharged (HR 1.10, 95%CI 1.02-

1.19). However, data showed no significant risk of mortality associated with an increased level of TropT (HR 1.00, 95%CI 1.00-1.01) (Table 2).

4. Discussion

The current study, conducted during South Africa's "second wave," found that COVID-19 patients admitted to ICU who died during the second COVID-19 wave had significantly elevated “D-dimer, TropT, NT-proBNP, CRP, and PaCO2” and low pH levels compared to those who were discharged from ICU during the second wave of the pandemic. In contrast there were no significant differences, none of the clinical features or co-morbidities were associated with the risk of death in the ICU.

Hypertension and diabetes were the most common co-morbidities. The increased $PaCO_2$ level of COVID-19 patients requires further investigation into the mean pH levels of COVID-19 patients (Elezagic et al., 2021). In COVID-19 patients, acidosis is thought to be caused by hypercapnia and multiorgan failure (Elezagic et al., 2021; Bezuidenhout et al., 2021). As the result, this could lower the pH level and has been linked to lower patient survival rates (Elezagic et al., 2021; Bezuidenhout et al., 2021; Skevaki et al., 2020). The mean pH. Of 7.41 among patients who died is relatively normal (range 7.35-7.45), showing that discharged patients were somewhat alkalotic (7.48). This is likely due to increased respiratory rate from COVID-19 pneumonia.

D-dimer is another important biomarker being studied as a potential prognostic factor of disease severity in COVID-19 (Zheng et al., 2020; Zhao et al., 2021). Elevated D-dimer levels indicate activation of the fibrinolytic system and the removal of clots or extravascular fibrin collections by plasmin (Zhao et al., 2021). In COVID-19 patients, an

increase in D-dimer could be a result from increased in inflammation, could a sign of thromboembolism, a potentially fatal consequence of hypercoagulation and fibrinolytic abnormalities (Zhao et al., 2021). In critically ill COVID-19 patients, pulmonary embolism (PE) and deep vein thrombosis (DVT) can cause respiratory failure (Chan et al., 2020; Cobre et al., 2021; Connors and Levy, 2020; Della et al., 2021; Helms et al., 2020; Ly et al., 2020; Zhao et al., 2021).

The positive relationship between D-dimer and the percentage of male patients in COVID-19 studies suggests that men are more severely affected than women when admitted to ICU (Zhao et al., 2021). Contrastingly, our study had more women than men admitted to the ICU during the second wave. This could be explained by pre-existing medical conditions which are found more in women such as comorbidities including hypertension, diabetes, and asthma; all of which are associated with D-dimer levels (Statsenko et al., 2021). Furthermore, four systemic complications, namely sepsis, secondary infection, disseminated intravascular coagulation (DIC), and coagulopathy, were found to be significantly associated with D-dimer (Ji et al., 2020). When we compared survival rates by biochemical covariate, we found that a lower D-dimer level was associated with a lower risk of mortality.

An elevated cardiac TropT level has a high specificity for cardiac injury and is a preferred biomarker of cardiac injury. The systematic review of eight studies including 1028 COVID-19 cases found an increased risk of severe COVID-19 patients with elevated TropT levels admitted in the ICU (RR 15.10, 95%CI 4.10 to 55.61, $P < 0.001$;) and the proportion of patients with elevated TropT in the survivors and non-survivor groups was 14.3% and 63.9%, respectively, showing higher proportion of non-survivors than survivors had

elevated TropT (RR 4.69, 95% CI 3.39 to 6.48, P < 0.001) (Li et al., 2020). Our results showed no significant association of mortality with elevated TropT. This could be because of the small sample size that was used in this study hence the need for further investigation with a large sample size.

Increased BNP and NT-proBNP secretion from the heart in response to high ventricular filling pressures is routinely used as a diagnostic and prognostic marker in heart failure and sometimes as a marker of the size or severity of ischaemic insults (Omland et al., 2002; Potter et al., 2009; Maisel et al., 2021; Zinellu et al., 2021). A recent systematic review of forty-four studies with 18,856 COVID-19 patients found a significant association between plasma BNP/NT-proBNP concentrations, disease severity, and mortality in these patients, which likely reflects the presence of cardiac involvement and its adverse sequelae in this group (Zinellu et al., 2021). Several studies have suggested that an increase in serum CRP levels is a reliable indicator of the presence and severity of SARS-CoV-2 infection (Kermali et al., 2020; Liu et al., 2020; Wang, 2020). A recent systematic review of eight studies and 2107 participants found moderate certainty that high blood CRP provides valuable prognostic information on mortality and/or severe disease in COVID-19 patients [16]. The same study showed mortality increased by 13.2% in severe COVID-19 patients with elevated CRP (Izcovich et al., 2020). In contrast, a meta-analysis of 13 studies found that elevated CRP was associated with severe COVID-19 and the need for ICU care, but not with mortality. Although there is no universal agreement on a cutoff point for determining COVID-19 severity, most studies used a 10 mg/L cutoff (Huang et al., 2020).

The study has several limitations. The study had a relatively small sample and was observational in nature and some of the clinical features and co-morbidities were reported as unknown. It was a single-center study and external validity is required to support the widespread use of our findings. In addition, a larger sample size might improve the statistical power of the study. However, our findings have significant implications for a better understanding of clinical presentations of COVID-19 severity in the ICU during the second wave.

5. Conclusion

In summary, this study found that demographic, clinical, and co-morbidity variables were not significantly associated with mortality among COVID-19 patients admitted to the ICU during the second wave. However, mortality was associated with the D-dimer, TropT and HCO3std. In addition, those who died had a shorter duration of ICU stay than those who survived. These findings may help development of a possible risk score to improve the identification of patients at high risk of mortality in the ICU and improve clinical decision-making in medical practice.

6. Abbreviations

COVID-19: coronavirus disease 2019; CRP: C-reactive protein; CVD: cardiovascular disease; ICU: Intensive care unit; LDH: Lactate dehydrogenase; DIC: disseminated intravascular coagulation; DVT: deep vein thrombosis; HIV: human immunodeficiency virus; LDH: Lactate dehydrogenase; NT-proBNP: N-terminal pro-B-type natriuretic peptide; $PaCO_2$: partial pressure of carbon dioxide; PE: pulmonary embolism; pH:

potential hydrogen; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; TropT: troponin T

7. Declarations

Ethics approval and consent to participate: The Investigators obtained ethical approval and waiver of consent from the Health Research Ethics Committee of the Faculty of Medicine and Health Sciences, Stellenbosch University, and Research Committee of the Tygerberg Hospital Ethics approval number N20/04/002_COVID-19.

Consent for publication: Not applicable.

Availability of data and material: The data presented in this study are available from the corresponding author upon request.

Competing interests: No conflict of interest declared.

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Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

The authors have no conflict of interest in this work.

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Table 1: Comparison of patient's characteristics among those who died or survived while admitted in the ICU

Factor	Level	Number	Total (82)	Discharge (28)	Death (54)	p-value
Age at diagnosis (yrs)		75		50.41 (39.89-60.54)	55.22 (47.20-58.07)	0.497
Gender	Female	82	55 (67%)	20 (71%)	35 (65%)	0.546
	Male		27 (33%)	8 (29%)	19 (35%)	
Smoking Status	Non-Smoker	82	41 (50%)	15 (54%)	26 (48%)	0.420
	Past Smoker		10 (12%)	3 (11%)	7 (13%)	
	Current Smoker		3 (4%)	0 (0%)	3 (6%)	
	Unknown		28 (34%)	10 (36%)	18 (33%)	
Septic shock	No	82	57 (70%)	17 (61%)	40 (74%)	0.360
	Yes		2 (2%)	0 (0%)	2 (4%)	
	Unknown		23 (28%)	11 (39%)	12 (22%)	
Fever	No	82	35 (43%)	14 (50%)	21 (39%)	0.999
	Yes		25 (30%)	5 (18%)	20 (37%)	
	Unknown		22 (27%)	9 (32%)	13 (24%)	
Myalgia	No	82	35 (43%)	14 (50%)	21 (39%)	0.122
	Yes		24 (29%)	5 (18%)	19 (35%)	
	Unknown		23 (28%)	9 (32%)	14 (26%)	
Nausea	No	82	57 (70%)	17 (61%)	40 (74%)	0.058
	Yes		2 (2%)	0 (%)	2 (4%)	
	Unknown		23 (28)	11 (39%)	12 (28%)	
Antibiotics	No		66 (80%)	25 (89%)	41 (76%)	0.190
	Yes		15 (18%)	3 (11%)	12 (22%)	
	Unknown		1 (1%)	0 (0%)	1 (2%)	
Acute kidney injury	No		49 (60%)	17 (61%)	32 (59%)	0.227
	Yes		12 (15%)	2 (7%)	10 (19%)	
	Unknown	82	21 (26%)	10 (36%)	19 (35%)	
Hypertension	No		29 (35%)	12 (43%)	27 (50%)	0.746
	Yes		39 (48%)	6 (21%)	8 (15%)	
	Unknown		14 (17%)			
Asthma	No	82	66 (80%)	21 (75%)	45 (83%)	0.546
	Yes		2 (2%)	1 (4%)	1 (2%)	
	Unknown		14 (17%)	6 (21%)	8 (15%)	
Diabetes mellitus	No	82	34 (41%)	10 (36%)	24 (44%)	0.604
	Yes		34 (41%)	12 (43%)	22 (41%)	
	Unknown		14 (17%)	6 (21%)	8 (15%)	
Hyperlipidaemia	No	82	63 (77%)	21 (75%)	42 (78%)	0.999

	Yes		5 (6%)	1 (4%)	4 (7%)	
	Unknown		14 (17%)	6 (21%)	8 (15%)	
HIV status	Negative	82	66 (80%)	26 (93%)	40 (74%)	0.470
	Positive		9 (11%)	2 (7%)	7 (13%)	
	Unknown		7 (9%)	0 (0%)	7 (13%)	
Anticoagulants	No	82	11 (13%)	2 (7%)	9 (17%)	0.314
	Yes		70 (85%)	26 (93%)	44 (81%)	
	Unknown		1 (1%)	0 (0%)	1 (2%)	
Corticosteroids	No	82	15 (18%)	4 (14%)	11 (20%)	0.560
	Yes		66 (80%)	24 (86%)	42 (78%)	
	Unknown		1 (1%)	0 (0%)	1 (2%)	
pH, median (IQR)		82	7.45 (7.39-7.49)	7.48 (7.46-7.50)	7.41 (7.31-7.46)	<0.001
$paCO_2$ (kpa), median (IQR)		82	5.5 (4.9-6.3)	5.05 (4.80-5.30)	6.00 (5.20-6.90)	<0.001
paO_2 (kpa), median (IQR)		82	8 (6.8-8.8)	8.05 (6.80-8.70)	7.95 (6.80-9.00)	0.950
$K^{+,}$ median (IQR)		82	4.3 (3.8-4.7)	4.15 (3.80-4.65)	4.40 (3.90-4.70)	0.305
Lactate, median (IQR)		82	1.6 (1.2-2.3)	1.40 (1.05-1.95)	1.65 (1.40-2.40)	0.074
HCO_3std, median (IQR)		74	28.25 (26.40-30.20)	28.20 (27.13-29.30)	28.40 (24.80-30.50)	0.937
SO2c, median (IQR)		82	91 (88-93)	92.50 (89.70-94.20)	90.20 (86.20-93.00)	0.084
PF Ratio, median (IQR)		82	72.68 (56.25-96.00)	84.22 (61.41-113.25)	68.39 (54.00-87.21)	0.052
Length of stay in hospital, median (IQR)		82	12 (8-17)	15.00 (9.50-20.00)	11.00 (7.00-16.00)	0.009
Temperature, median (IQR)		82	37.1 (36.7-37.8)	37.20 (36.80-38.10)	37.10 (36.70-37.80)	0.91
D-dimer, median (IQR)		82	1.03 (0.41-3.91)	0.41 (0.24-0.95)	1.51 (0.65-4.86)	<0.001
HbA1c, median (IQR)		72	7.6 (6.3-8.8)	7.80 (6.30-11.60)	7.50 (6.30-8.60)	0.348
Platelets, median (IQR)		76	309 (240-383)	321.50 (250.00-412.50)	275.00 (240.00-366.50)	0.277

TropT, median (IQR)		58	13 (6-27)	6.00 (4.00-15.00)	18.00 (9.00-40.00)	0.001
NTProBNP, median (IQR)		54	178.5 (89-791)	110.00 (43.00-230.00)	254.50 (119.00-1467.00)	0.007
CRP, median (IQR)		73	148.00 (89.00-224.00)	106.00 (67.00-198.00)	167.50 (120.00-237.00)	0.010

Abbreviations: Abbreviations: BMI: Body Mass Index, HIV: human immunodeficiency virus, HbA1c: Haemoglobin A1C , K^+: potassium, NTProBNP: N-terminal pro b-type natriuretic peptide, CRP: C-reactive protein, $paCO_2$: partial pressure of carbon dioxide, pH: potential hydrogen, PaO_2: partial pressure of oxygen, $PaCO_2$: partial pressure of carbon dioxide, SaO_2: Arterial oxygen saturation, TropT: Troponin T, HCO_3std: standard bicarbonate is PF ratio: Arterial partial pressure of oxygen (in mmHg) / Inspired oxygen concentration; P-value computed without considered of unknowns and for smoking status past and current smoker considered as one group

Table 2: Comparison of Cox proportional HR in relation to the risk of discharge and death

	Discharge				Death			
	PHR	**SD**	**2.5**	**97.5**	**PHR**	**SD**	**2.50**	**97.50**
Age category								
<50	Reference							
50-59	0.73	2.22	0.15	3.49	0.97	1.62	0.37	2.46
>=60	0.62	1.95	0.16	2.21	0.96	1.53	0.42	2.22
HIV								
Negative	Reference							
Positive	0.94	2.54	0.13	5.11	1.72	1.66	0.61	4.48
hypertension								
No								
Yes	0.80	2.07	0.19	3.20	1.07	1.54	0.46	2.46
Gender								
Male	Reference							
Female	1.98	2.05	0.46	7.81	1.65	1.50	0.74	3.62
Hyperlipidaemia								
No								
Yes	1.02	3.74	0.06	10.31	1.19	1.96	0.30	4.13
Diab_mellitus								
No								
Yes	1.51	2.09	0.33	6.03	0.73	1.56	0.30	1.72
Asthma								
No								
Yes	4.11	3.54	0.27	38.92	2.30	3.02	0.20	15.32
Continuous variables								
PF_ratio	1.00	1.00	0.99	1.01	1.00	1.00	0.99	1.00
so2c	1.02	1.04	0.96	1.12	0.98	1.01	0.96	1.00

PTT Ratio	2.10	1.53	0.89	4.73	0.92	1.39	0.47	1.71
D-Dimer	0.86	1.09	0.71	0.99*	1.05	1.03	1.00	1.11*
TropT	0.96	1.03	0.90	1.01	1.00	1.00	1.00	1.01*
Lymphocytes	1.10	1.04	1.02	1.19*	0.98	1.03	0.93	1.03
BMI	0.53	1.69	0.18	1.45	0.66	1.43	0.33	1.34
Platelets	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
hco3std	0.96	1.04	0.90	1.03	0.96	1.02	0.93	0.99*
HbA1c	1.01	1.09	0.85	1.19	1.08	1.06	0.96	1.21

Abbreviations: Abbreviations: BMI: Body Mass Index, HIV: human immunodeficiency virus, NTProBNP: N-terminal pro b-type natriuretic peptide, CRP: C-reactive protein, $paCO_2$: partial pressure of carbon dioxide, pH: potential hydrogen, PaO_2: partial pressure of oxygen, $PaCO_2$: partial pressure of carbon dioxide, SaO_2: Arterial oxygen saturation, TnT: Troponin T, HCO_3std: standard bicarbonate is PF ratio: Arterial partial pressure of oxygen (in mmHg) / Inspired oxygen concentration , PHR: posterior hazard ratio